June 23, 2005

8EHQ-0605-15946S

REDACTED VERSION

Document Control Office (7407W)
U.S. Environmental Protection Agency
ATTN: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
1200 Pennsylvania Ave., NW
Washington, DC 20004-3302

Company Sanitized

Subject: 8EHQ-05-15946

Dear Sir or Madam:

This notice amends the American Chemistry Council Terephthalates Panel's[1] previous submission (8EHQ-05-15946), dated March 7, 2005. In the 03/07/05 notice, we provided data from a multigeneration reproduction toxicity study of terephthalic acid, CAS Registry number 100-21-0. The Panel is now forwarding the narrative portion of the study and is being submitted to EPA as confidential business information in accordance with EPA's requirements for protecting the same.

Confidentiality Statement

This letter contains confidential business information. These claims are pursuant to §14 of TSCA and to 40 CFR Part 2. No public disclosure may be made of information in this letter that has been claimed confidential absent prior notification and opportunity to respond by the American Chemistry Council pursuant to 40 CFR Part 2.

[Responses for Substantiation of CBI redacted}

If you have any questions please contact Dr. Has Shah of the American Chemistry Council at (703) 741-5637 or via e-mail at Has_Shah@americanchemistry.com

SANITIZED VERSION

CENTRAL TOXICOLOGY LABORATORY
ALDERLEY PARK MACCLESFIELD
CHESHIRE UK

CTL/RR0915/REGULATORY/REPORT

TEREPHTHALIC ACID: MULTIGENERATION REPRODUCTION TOXICITY STUDY IN RATS

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TEREPHTHALIC ACID: MULTIGENERATION REPRODUCTION TOXICITY STUDY IN RATS

STUDY DETAILS

Sponsor:	BP Chemicals Limited. Chertsey Road, Sunbury-on-Thames Middlesex, TW16 7LN, UK.
Sponsor Reference:	CO0483
CTL Test Substance Reference Number:	Y00751/004
CTL Study Number:	RR0915 (F0 generation) RR0915 (F1 generation)
Document Number:	CTL/RR0915/REG/REPT

AUTHOR

G M Milburn

DATE OF ISSUE

20 January 2003

STATEMENT OF DATA CONFIDENTIALITY CLAIM

THIS DOCUMENT CONTAINS INFORMATION CONFIDENTIAL AND TRADE SECRET TO BP CHEMICALS LIMITED

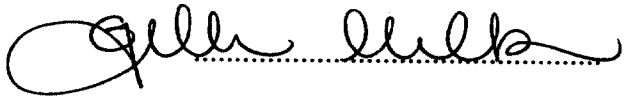
It should not be disclosed in any form to an outside party, nor should information contained herein be used by a registration authority to support registration of this product or any other product without the written permission of BP Chemicals Limited.

STATEMENT OF GLP COMPLIANCE AND AUTHENTICATION

I, the undersigned, declare that the objectives laid down in the protocol were achieved and that the data generated are valid. The report fully and accurately reflects the procedures used and the raw data generated in the above study.

The study (RR0915) was conducted in compliance with the UK Principles of Good Laboratory Practice (The United Kingdom GLP Regulations 1999, Statutory Instrument No. 3106). These Principles are in accordance with the OECD Principles of Good Laboratory Practice, revised 1997 (ENV/MC/CHEM(98)17).

G M Milburn
Study Director



20 January 2003
Date

This page
may be required
by some
regulatory authorities.

QUALITY ASSURANCE STATEMENT

In accordance with CTL policy and QA procedures for Good Laboratory Practice, this report has been audited and the conduct of this study has been inspected as follows:

Date	Audit/Inspection	Date of QA Report
30 Apr 2001	Protocol	10 May 2001
23 May 2001	Dose preparation	23 May 2001
25 May 2001	Randomisation	29 May 2001
11 Aug 2001	Pairing	13 Aug 2001
05 Sep 2001	Pup sexing, bodyweights, clinical observations, landmark monitoring	06 Sep 2001
19 Sep 2001	Landmark monitoring	19 Sep 2001
03 Oct 2001	Selection of pups	03 Oct 2001
03 Oct 2001	Post mortem	03 Oct 2001
01 Nov 2001	Dose analysis	01 Nov 2001
21 Nov 2001	Parent bodyweights, clinical observations, food weighing	21 Nov 2001
04 Dec 2001	Vaginal smears	04 Dec 2001
06 Feb 2002	Post mortem	06 Feb 2002
21 Feb 2002	Post mortem	21 Feb 2002
12 Mar 2002	Sperm analysis	12 Mar 2002
21 Mar 2002	Sperm analysis	21 Mar 2002
19 Apr 2002	Quantitative evaluation of primordial follicles	19 Apr 2002
27 Jun 2002	Draft report	22 Jul 2002
09 Oct 2002	Draft report	07 Nov 2002
14 Jan 2003	Final report review	16 Jan 2003

Facilities and process based procedures associated with this study were inspected in accordance with QA Standard Operating Procedures.

So far as can be reasonably established, the methods described and the results given in the final report accurately reflect the raw data produced during the study, RR0915.

I F Bayliss ..... 20 January 2003

(CTL Quality Assurance Unit)

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STUDY CONTRIBUTORS

The following contributed to this report in the capacities indicated:

Name	Title
G M Milburn	Study Director, CTL
R W Lewis	Study Reviewer
Z Welsh	Statistician
E Riley	Formulation Analyst
S F Moreland	Pathologist

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TSCA Confidential Business Information

This page is provided for the Regulatory Authority Reviewer's notes.

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1. SUMMARY

1.1 Study design

Groups of 26 male and 26 female (F0 parents) weanling Alpk:APfSD (Wistar-derived) rats were fed diet containing 0 (control), 1000, 5000 or 20000 ppm terephthalic acid. After 10 weeks, the animals were mated and allowed to rear the ensuing F1 litters to weaning. The breeding programme was repeated with the F1 parents selected from the F1 pups to produce the F2 litters after a 10-week pre-mating period. Test diets were fed continuously throughout the study.

The growth of the parental generation, reproductive function, mating behaviour, conception, gestation, parturition, lactation and weaning and the growth and development of the pup were determined.

1.2 Results

Bodyweights were reduced in F0 males, F0 females receiving 20000 ppm terephthalic acid (during gestation and *post partum)* and in F1 males and females. Weights of animals receiving 1000 or 5000 ppm terephthalic acid were similar to controls throughout the study.

Food consumption of F1 males and females receiving 20000 ppm was generally lower than that of controls. Food utilisation was less efficient than control in the 20000 ppm group in both generations.

There were no effects on smear cycle and pattern, pre-coital interval, gestation length, proportion of successful matings, pups live born, litter size, pup survival, pup sex distribution or pup clinical observations in any treated group.

Bodyweights of F1 pups receiving 20000 ppm terephthalic acid were reduced from day 15 *post partum.* Bodyweights of F2 males and females in the 20000 ppm treatment group were lower than control at all timepoints which correlated with increased litter sizes compared to control. Total litter weight was not different across all groups. Bodyweights of F1 males receiving 5000 ppm were lower than controls on day 29 *post partum.* Bodyweights of F2pups receiving 5000 ppm were lower than control from day 15 *post partum.* There was no effect on pup weight in the 1000 ppm group.

There was a statistically significant decrease in the ano-genital distance of females only in the F1 and F2 litters in the 20000 ppm dose group. Ano-genital distances in the 1000 and 5000 ppm females and in all male groups were similar to those of controls. Vaginal opening was slightly delayed, by 1.6 days, in F1 females in the 20000ppm group. Preputial separation was delayed in F1 males in the 5000 and 20000 ppm groups (by 0.8 days and 1.6 days respectively). These differences were related to the reduced bodyweight of these animals.

Kidney weights (both absolute and adjusted for bodyweight) were decreased in males from all treated male groups in both generations. Effects in females were less consistent and generally only absolute kidney weight were reduced. Relative liver weights were increased in both sexes and both generations in the 20000 ppm group only.

There were no effects on sperm number, sperm motility or sperm morphology.

The number of decedent F0 and F1 animals was very low and the incidence was unrelated to dose level. There was no effect of treatment on the number of mated F0 or F1 animals failing to produce litters and no changes were detected in the reproductive organs which could be attributed to treatment.

A variety of changes were observed in the urinary bladder of animals of both sexes receiving 20000 ppm terephthalic acid. The incidence in the F1 animals was greater than in the F0. It is considered that these changes are related to treatment and indicate an irritant effect of the compound on the bladder mucosa. Bladders were not examined from animals receiving 1000 or 5000 ppm. Minimal or slight renal papillary necrosis was observed in the grossly abnormal kidneys of a few males (2 F0 and 2 F1) receiving 20000 ppm terephthalic acid. This is an uncommon spontaneous finding and it is considered that this lesion is likely to be related to treatment. Only macroscopically abnormal kidneys were examined.

1.3 Conclusion

Dietary administration of 20000 ppm terephthalic acid for two successive generations did not result in any effects on reproductive performance. No gross or microscopic changes were seen in the reproductive system that could be related to terephthalic acid administration.

Irritant changes were observed in the bladder of males and females receiving 20000 ppm terephthalic acid and there was some evidence for an effect on the kidney at this dose level. These tissues were not examined for the 1000 or 5000 ppm groups.

Reductions in pup bodyweight generally occurred from day 15 post partum, when the offspring had started consuming solid diet, and are considered to be a direct effect of the test material on the pups rather than an expression of developmental toxicity. Pup bodyweights in the F2 generation of the 20000 ppm treatment group were lower than control from parturition, but this is considered to be related to the larger litter size in this group.

The only effect at a dose level of 1000 ppm was a decrease in kidney weight in adults and pups.

The no observed adverse effect level (NOAEL) for effects on reproduction and development was 20000 ppm, the highest dose used in this study.